

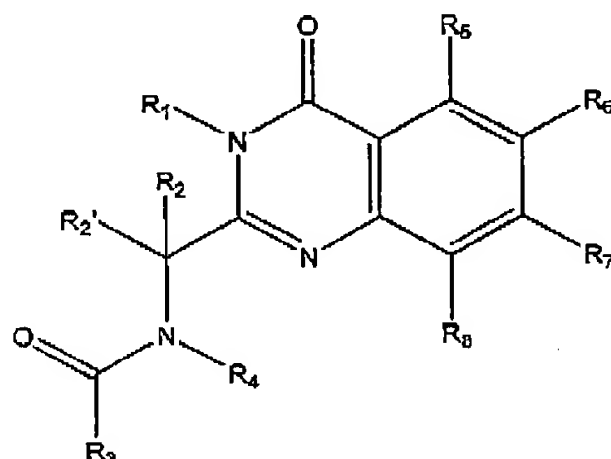
U.S. Application No. 09/724,778
Attorney Docket Number 09367.0018-06000
(formerly CYTOP00901)

In the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1-17. (Cancelled)

18. (Previously Presented) A method of treating cancer comprising administering a therapeutically effective dose of a compound having the structure of:



wherein

R₁ is benzyl or halobenzyl;

R₂ is chosen from ethyl and propyl;

R₂' is hydrogen;

R₃ is substituted phenyl;

R₄ is (CH₂)_m OH or (CH₂)_p R₁₆ wherein m is 2 or 3 and p is 1-3;

R₅ is hydrogen;

R₆ is hydrogen;

R₇ is halo;

R₈ is hydrogen;

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R_{16} is chosen from amino, propylamino, and azetidiny1;
or a pharmaceutically acceptable salt of any of the foregoing compounds,
wherein said therapeutically effective dose is an amount effective to inhibit KSP.

19. (Original) A method according to claim 18 wherein the stereogenic center to which R_2 and $R_{2'}$ are attached is of the R configuration.

20-64. (Cancelled)

65. (Previously presented) The method of claim 18, wherein

R_1 is benzyl;

R_2 is isopropyl;

$R_{2'}$ is hydrogen;

R_3 is p-tolyl;

R_4 is 3-aminopropyl;

R_5 is hydrogen;

R_6 is hydrogen;

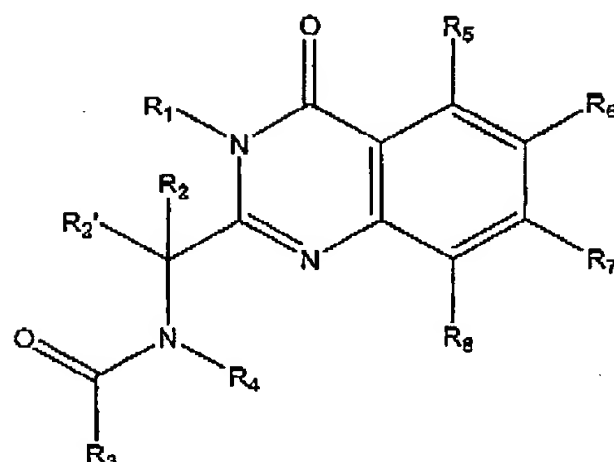
R_7 is chloro; and

R_8 is hydrogen.

66. (Cancelled)

67. (Previously Presented) A method of treating cancer comprising administering a therapeutically effective dose of a compound having the structure of:

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wherein

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-tolyl; R₄ is 3-(isopropylamino)propyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is p-chlorobenzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-bromophenyl; R₄ is 2-(dimethylamino)ethyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-tolyl; R₄ is 3-(dimethylamino)propyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-tolyl; R₄ is 3-aminopropyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is m-methoxybenzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-tolyl; R₄ is 3-aminopropyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-bromophenyl; R₄ is 3-aminopropyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is isopropyl; R₂' is hydrogen; R₃ is p-tolyl; R₄ is 3-aminopropyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-tolyl; R₄ is azetidin-3-ylmethyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-tolyl; R₄ is 2-aminoethyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-bromophenyl; R₄ is 2-aminoethyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

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R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-tolyl; R₄ is 3-aminopropyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-tolyl; R₄ is 2-(methylamino)ethyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-bromophenyl; R₄ is 3-(methylamino)propyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-bromophenyl; R₄ is 2-(methylamino)ethyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-tolyl; R₄ is azetidin-2-ylmethyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-bromophenyl; R₄ is 3-aminopropyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is methylsulfinylmethyl; R₂' is hydrogen; R₃ is p-tolyl; R₄ is 3-aminopropyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-tolyl; R₄ is piperidin-3-ylmethyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-tolyl; R₄ is 3-aminopropyl; R₅, R₆, and R₈ are hydrogen; and R₇ is fluoro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-bromophenyl; R₄ is 2-(dimethylamino)ethyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-tolyl; R₄ is 2-aminoethyl; R₅, R₆, R₇ and R₈ are hydrogen;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-tolyl; R₄ is piperidin-2-yl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-bromophenyl; R₄ is 4-aminobutyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is m-chlorobenzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-bromophenyl; R₄ is 2-(dimethylamino)ethyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-bromophenyl; R₄ is 2-(dimethylamino)ethyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

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R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-tolyl; R₄ is 2-(piperidin-1-yl)ethyl;
R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-tolyl; R₄ is 2-(imidazol-3-yl)ethyl; R₅,
R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-tolyl; R₄ is pyrrolidin-3-ylmethyl; R₅,
R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-bromophenyl; R₄ is
2-(diethylamino)ethyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-tolyl; R₄ is 2-(dimethylamino)ethyl;
R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-chlorophenyl; R₄ is
2-(dimethylamino)ethyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-tolyl; R₄ is 4-aminobutyl; R₅, R₆, and
R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-tolyl; R₄ is pyrrolidin-2-ylmethyl; R₅,
R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-tolyl; R₄ is 3-(azetidin-1-yl)propyl;
R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-tolyl; R₄ is 2-(pyrrolidin-1-yl)ethyl;
R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-tolyl; R₄ is 3-(pyrrolidin-1-yl)propyl;
R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-bromophenyl; R₄ is 3-
(dimethylamino)propyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is propyl; R₂' is hydrogen; R₃ is p-bromophenyl; R₄ is 2-
(dimethylamino)ethyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-bromophenyl; R₄ is 2-(pyrrolidin-1-
yl)ethyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-bromophenyl; R₄ is 3-(pyrrolidin-1-
yl)propyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

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R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-tolyl; R₄ is piperidin-4-ylmethyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is methylsulfinylethyl; R₂' is hydrogen; R₃ is p-tolyl; R₄ is 3-aminopropyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-tolyl; R₄ is 3-(piperidin-1-yl)propyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is benzyl; R₂' is hydrogen; R₃ is p-tolyl; R₄ is 3-aminopropyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-bromophenyl; R₄ is (N-ethylpyrrolidin-2-yl)methyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-tolyl; R₄ is 3-piperidinyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-tolyl; R₄ is 4-piperidinyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is p-chlorobenzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-bromophenyl; R₄ is 2-(dimethylamino)ethyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-bromophenyl; R₄ is 2,2-dimethyl-3-(dimethylamino)propyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-bromophenyl; R₄ is 5-aminopentyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-tolyl; R₄ is 3-(dimethylamino)propyl; R₅, R₆, and R₈ are hydrogen; and R₇ is fluoro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-bromophenyl; R₄ is 3-(2-methylpiperidin-1-yl)propyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-tolyl; R₄ is 2-(dimethylamino)ethyl; R₅, R₆, and R₈ are hydrogen; and R₇ is fluoro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-bromophenyl; R₄ is 2-(N-methylpyrrolidin-2-yl)ethyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-trifluoromethylphenyl; R₄ is 3-(dimethylamino)propyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

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R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-bromophenyl; R₄ is 3-(diethylamino)propyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-bromophenyl; R₄ is 3-(N-methylpiperazin-1-yl)propyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is 4-(CBZ)aminobutyl; R₂' is hydrogen; R₃ is p-tolyl; R₄ is 3-aminopropyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-bromophenyl; R₄ is aminoethoxyethyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is 2-naphthyl; R₄ is 2-(dimethylamino)ethyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is cyclohexylmethyl; R₂' is hydrogen; R₃ is p-tolyl; R₄ is 3-aminopropyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-bromophenyl; R₄ is 2-(piperidin-1-yl)ethyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-tolyl; R₄ is 3-hydroxypropyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-fluorophenyl; R₄ is 2-(dimethylamino)ethyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-bromophenyl; R₄ is 6-aminoethyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-tolyl; R₄ is 2-(dimethylamino)ethyl; R₅, R₇, and R₈ are hydrogen; and R₆ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-bromophenyl; R₄ is 2-(dimethylamino)ethyl; R₅, R₆, and R₈ are hydrogen; and R₇ is fluoro;

R₁ is benzyl; R₂ is methyl; R₂' is hydrogen; R₃ is p-bromophenyl; R₄ is 2-aminoethyl; R₅, R₆, R₇ and R₈ are hydrogen;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-tolyl; R₄ is 2-(dimethylamino)ethyl; R₅, R₆, and R₇ are hydrogen; and R₈ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-bromophenyl; R₄ is 2-(dimethylamino)ethyl; R₆, R₇, and R₈ are hydrogen; and R₅ is chloro;

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R₁ is benzyl; R₂ is aminobutyl; R₂' is hydrogen; R₃ is p-tolyl; R₄ is 3-aminopropyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-tolyl; R₄ is 2-(dimethylamino)ethyl; R₅ and R₈ are hydrogen; and R₆ and R₇ are fluoro;

R₁ is m-tolyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-bromophenyl; R₄ is 2-(dimethylamino)ethyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro;

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-bromophenyl; R₄ is 2-(dimethylamino)ethyl; R₅ and R₈ are hydrogen; and R₆ and R₇ are fluoro; or

R₁ is benzyl; R₂ is ethyl; R₂' is hydrogen; R₃ is p-bromophenyl; R₄ is 2-carboxyethyl; R₅, R₆, and R₈ are hydrogen; and R₇ is chloro,

or a pharmaceutically acceptable salt of any of the foregoing compounds,
wherein said therapeutically effective dose is an amount effective to inhibit KSP.

68-75. (Cancelled)

76. (Previously Presented) The method of claim 18, wherein R₃ is phenyl substituted with one or more halo, lower alkyl, lower alkoxy, nitro, carboxy, methylenedioxy, or trifluoromethyl.

77-81. (Cancelled)

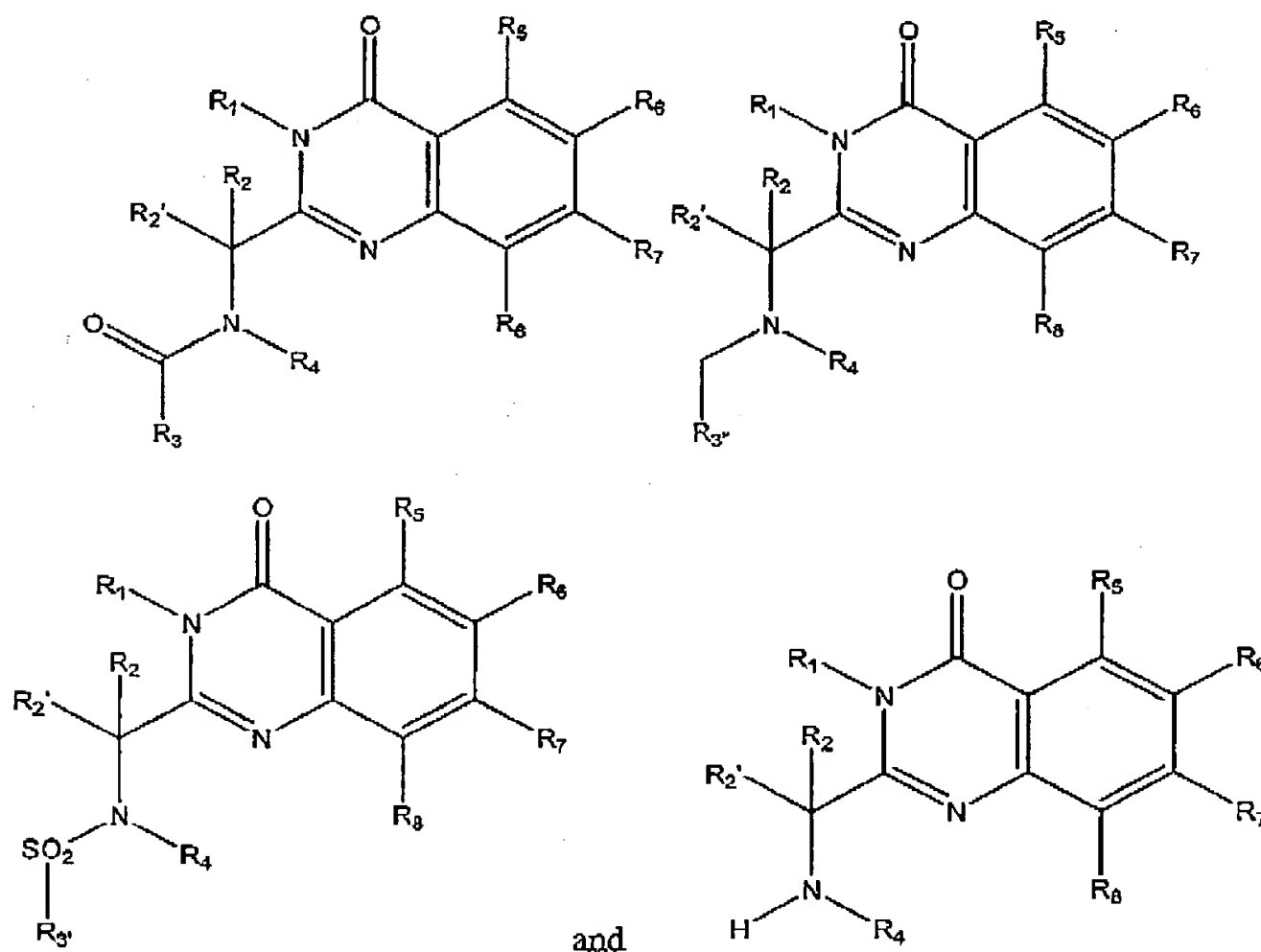
82. (Previously Presented) The method of claim 18, wherein said salt is a mesylate.

83. (Cancelled)

84. (Previously Presented) A method according to claim 67 wherein the stereogenic center to which R₂ and R₂' are attached is of the R configuration.

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85. (New) A method of inhibiting mitosis in a cell comprising contacting the cell with a compound chosen from the group consisting of:



wherein:

R_1 is chosen from hydrogen, alkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl, and substituted alkylheteroaryl;

R_2 and R_2' are independently chosen from hydrogen, alkyl, and substituted alkyl;

R_3 is chosen from hydrogen, alkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl, substituted alkylheteroaryl, and $R_{15}NH-$

$R_{3'}$ is chosen from hydrogen, alkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl, and substituted alkylheteroaryl;

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R₃ is chosen from alkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl, and substituted alkylheteroaryl;

R₄ is chosen from hydrogen, alkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl, and substituted alkylheteroaryl;

R₅, R₆, R₇ and R₈ are independently chosen from hydrogen, alkyl, alkoxy, halogen, fluoroalkyl, nitro, dialkylamino, alkylsulfonyl, alkylsulfonamido, sulfonamidoalkyl, sulfonamidoaryl, alkylthio, carboxyalkyl, carboxamido, aminocarbonyl, aryl and heteroaryl; and

R₁₅ is chosen from alkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl, and substituted alkylheteroaryl.

86. (New) The method of claim 85 wherein R₁ is an optionally substituted aryl group.

87. (New) The method of claim 85 wherein R₂ is hydrogen and R₂ is hydrogen, lower alkyl or substituted lower alkyl.

88. (New) The method of claim 85 wherein R₃ is R₁₅NH-.

89. (New) The method of claim 85 wherein R₃ is optionally substituted aryl.

90. (New) The method of claim 85 wherein R₃ is substituted phenyl.

91. (New) The method of claim 85 wherein R₄ is optionally substituted alkyl.